

Can partial splenectomy preserve humoral immunity in pediatric patients? Risks and benefits of partial splenectomy

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ABSTRACT

The spleen plays an important role in removing normal and abnormal cells from the blood and in providing an immunologic response to encapsulated bacteria. Surgical splenectomy provides effective treatment for several pediatric disorders, such as congenital and acquired hemolytic anemias, abdominal traumas and immunological and metabolic disorders, but it is associated with an immediate and lifelong risk of overwhelming infection. An alternative to conventional splenectomy is partial splenectomy, recommended especially in children younger than 5 years of age. Recommendations for the prevention of overwhelming post-total splenectomy infection include: Pneumococcal, Haemophilus influenzae type B and Meningococcal immunizations, antimicrobial prophylaxis and prompt antibiotic treatment of acute febrile illness; conversely, there is no clear evidence indicating which prevention measures are to be performed in patients undergoing partial splenectomy.

Key words: partial splenectomy, children, immunization

SPLEEN PHYSIOLOGY

It was initially accepted that the spleen not only filters blood but is an important regulation center for the body's immune-metabolic-endocrine network. (1,2) The spleen is part of the lymphatic system. It is thought to be central in regulating the immune system, but it plays also a metabolic

role for its involvement in endocrine function. Immune function (through phagocytosis, but also through T cell-mediated immunity and B cell-mediated humoral immunity) is the most important function of the spleen. (3) The spleen is one of the centers of activity of the reticulo-endothelial system and can be considered analogous to a large lymph node, as its absence leads to a predisposition toward certain infections. (4,5) It is involved in the production of opsonins, properdin, and tuftsin, which facilitate bacterial phagocytosis. Another function of the spleen is the creation of red blood cells and lymphocytes (extramedullary hematopoiesis). (4) The spleen has a reservoir function, consisting of 40 ml of blood, one third of produced platelets, margined neutrophils, and factor VII. It is also involved in the catheresis of white blood cells, red blood cells and platelets, old or damaged (culling), and in the removal of Howell-Jolly bodies from red blood cells (pitting) and parasites. (6)

INDICATIONS FOR SPLENECTOMY

The many indications for splenectomy can be divided into medical (hematologic) and surgical categories. (7-9) Medical indications are currently: congenital hemolytic anemia, in which red cell abnormalities promote splenic hemolysis (hereditary spherocytosis (HS), elliptocytosis, pyruvate kinase deficiency, sickle cell disease); acquired immune disorders, in which red cells or platelets are targeted for splenic destruction by being coated with autoan-

tibodies (autoimmune thrombocytopenia (ITP), chronic autoimmune hemolytic anemia); hypersplenism, in which a hypertrophied spleen becomes a red cell trap (thalassemia major, congestive splenomegaly, splenomegaly from accumulation, as in Gaucher's disease and Niemann-Pick). Surgical indications include: traumatic rupture; left abdominal interventions, intrinsic splenic diseases (cysts, primitive tumors). Splenectomy is the only rational therapy for symptomatic hereditary spherocytosis and hereditary elliptocytosis. It is also performed in most spleen ruptures and tears. In other cases, it must be evaluated on a case-by-case basis. The accepted indication for splenectomy in thalassemia is an annual demand for blood of one and a half times more than in patients with splenectomy or a blood consumption of 200 ml/kg/year. Splenectomy is indicated in symptomatic chronic ITP taking into account that patients with very low platelet counts are at risk for a bleeding diathesis leading to subarachnoid, intracerebral hemorrhage or other internal bleeding". Thrombocytopenia should last at least be severe ($<10.000/\text{mm}^3$) and symptomatic.

PROPHYLAXIS POST SPLENECTOMY

All splenectomized patients should receive additional vaccinations due to the high risk of developing invasive infections by encapsulated bacteria (table 1). In elective splenectomy, vaccinations should be carried out at least 2 weeks before the pro-

Table 1. Guidelines on the prophylaxis of splenectomized patients (from AIEOP guidelines)

Prophylaxis by vaccination	Antibiotic oral prophylaxis	Parenteral antibiotic prophylaxis	Empirical fever therapy
Anti-streptococcus pneumoniae (PPSV23 E PCV7)	Penicillin V 125 mg twice daily (<3 or 5 years)	Penicillin G benzathine 600.000 U every 3-4 weeks i.m. (weight < 27 kg)	Amoxicillin-Clavulanic acid 25 mg/kg twice daily (max 1 g three times daily)
Anti-Haemophilus (PRP-T; PRP-D; HbOC; PRP-OMP)	Penicillin V 250 mg twice daily (3 or 5 -14 years)	Penicillin G benzathine 1.200.000 U every 3-4 weeks i.m. (weight > 27 kg)	Ceftriaxone 80 mg/kg i.v. once daily (max 2 g)
Anti-Neisseria meningitidis (tetraivalent)	Penicillin V 250/500 mg twice daily (adults)		Vancomycin 30 mg/kg/day i.v. in 4 doses (max 2 g per day) for resistant penicillin pneumococcus

AIEOP, Associazione Italiana Ematologia ed Oncologia Pediatrica.

cedure and are more effective in children over 2 years of age. Vaccinations can be administered even after the intervention, in case of emergency splenectomy, probably with lower efficacy. (10) The pneumococcal vaccine protects against the most common strains. The anti- Haemophilus influenzae type B vaccination is certainly indicated in patients at risk, even if no data is available with respect to persistence of immunity. The anti-meningococcal vaccine is poorly immunogenic and confers immunity of short duration because the rate of vaccine-induced antibodies tends to drop significantly after 2-3 years of vaccination. Its administration in asplenic children is therefore not routinely recommended; it can be prescribed for journeys to Nepal, India and Sub-Saharan Africa. Since vaccination does not allow complete coverage against pathogens in asplenic subjects, antibiotic prophylaxis is recommended. In certain patients this may be necessary throughout their life, or at least for the first two years after surgery. Despite prophylaxis, infections are possible from resistant strains; hence, in the case of fever or signs of severe infection, drug therapy is commenced "empirically", targeted towards pathogens suspected to be the cause of the episode. Other preventive measures include: avoiding malarial areas, avoiding dog bites, and prevention of thrombotic risk with an antiplatelet agent, if platelet levels are very high (greater than 1000000 platelets / mm3). (11-13)

DISCUSSION

Because of the risk of post-splenectomy sepsis, subtotal (or partial) splenectomy has been advocated as an alternative procedure. (14) The spleen plays a vital role in the host defense against infection as a component of the reticuloendothelial system. (15,16) At birth, the infant has circu-

lating antibodies due to trans-placentally acquired IgG from the mother. These IgG antibodies disappear during the first 6 months of life, and for the next 2 years most infants lack circulating antibodies. This reflects the period of greatest risk of contracting invasive infections by encapsulated bacteria. In children younger than 5 years of age, the risk of serious infection is 10% versus a 1-2% risk in adults. Two thirds of infections occur within 2-3 years after splenectomy. A third occurs within 5 years, but there have also been cases of fulminant infections even after 20 years. Several authors recommend performing a partial splenectomy in children under 5 years of age, as a major preventive measure against overwhelming post-splenectomy infection (OPSI), and subsequently a total splenectomy, if necessary. (17,18)

Van Wyck et al., have reported that preservation of a splenic remnant, approximately one-third the size of the normal spleen, seems critical to maintaining this protective effect in the rat. (19-21) Several authors have confirmed the effectiveness of partial splenectomy in the treatment of children with mild to moderate HS, reserving total splenectomy for severe disease. (14)

Partial splenectomy is a viable option for selected patients with HS leading to improvement in hematologic and clinical abnormalities. Although a variable rate of regrowth following partial splenectomy has been described, it is not necessarily correlated with recurrent hemolysis. So partial splenectomy can be performed in these patients, with minimal morbidity and good results. (22-24) In Shilling et al., splenectomy is not suggested in patients with mild or moderate anemia. (25)

Partial splenectomy, with preservation of around 25% of the normal spleen volume, is a safe and effective procedure for retaining immune competence in patients with thalassemia and it should be considered a major preventive measure against OPSI,

especially when access to Pneumococcal immunizations (effective and mandatory measure against OPSI), or compliance with continuous oral antibiotics is not optimal. Splenic regeneration after partial resection or implantation is much more limited and eutopic remnants provide protection against blood born pneumococcal challenges, relative to the remnant size (19); Marques et al. suggest that the autotransplanted spleen does not sequester damaged red blood cells in the same manner as the regenerated spleen after partial resection. (26) This is because in the autotransplanted spleen there is a reduction in white pulp, which is the principal location of the fixed macrophages and the site of phagocytosis of pneumococci within the spleen. Therefore, preservation of a splenic remnant with an intact blood supply remains preferable to autotransplantation as a means to conserve functional splenic function.

The approach to the management (prevention and treatment) of infectious complications is currently very empirical and generally based on studies carried out in patients with sickle cell disease or single case reports. This has often led not only to contrasting practices, but also misunderstandings from a clinical point of view, because decisions are often based on personal feelings and not on objective scientific data.

Despite several authors agreeing on the increased effectiveness of partial splenectomy in preserving the immune function of the spleen, especially in children under 5 years of age, there is no clear evidence to support this at the present time. For this reason, some authors recommend immunization against S. Pneumoniae, Haemophilus Influenzae, and in certain cases Neisseria Meningitidis before partial splenectomy, followed by antibiotic prophylaxis (penicillin) for 1 year after the procedure. (14,27)

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